No. 04-607

FILED
FEB 6 - 2006
OFFICE OF THE CLERK
SUPREME COURT, U.S.

In The
Supreme Court of the United States

LABORATORY CORPORATION OF AMERICA HOLDINGS (DOING BUSINESS AS LABCORP),

Petitioner,

v.

METABOLITE LABORATORIES, INC. AND COMPETITIVE TECHNOLOGIES, INC.,

Respondents.

On Writ Of Certiorari To The United States Court Of Appeals For The Federal Circuit

BRIEF FOR *AMICI CURIAE* PERLEGEN SCIENCES, INC. AND MOHR, DAVIDOW VENTURES IN SUPPORT OF RESPONDENTS

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INTEREST OF *AMICI CURIAE*[1]

Amicus Perlegen Sciences, Inc. ("Perlegen") is a leader in personalized medicine, working to provide safe and effective medications to patients worldwide. The company quickly and cost effectively analyzes millions of unique genetic variations in patients to explain and predict the efficacy and adverse effect profiles of prescription drugs. For example, if a sub-group of patients is resistant to, or adversely affected by, a drug, the company can determine the genetic basis for such resistance or adverse effect, and thereby identify the population for whom the drug would be both safe and effective. The company also applies this expertise to discovering genetic variants associated with disease and thereby pave the way for new therapeutics and diagnostics. Through its rapid ability to examine entire genomes, Perlegen is attempting to bring drugs to market whose clinical development would otherwise have been discontinued and to find the genetic associations with drug response and disease that improve patient care.

Perlegen has a strong interest in ensuring that claim 13 ("Claim 13") of U.S. Patent No. 4,940,658 (the "'658 patent") is held to recite patentable subject matter. A holding that the diagnostic method identified in Claim 13 is unpatentable could significantly diminish Perlegen's incentive to engage in research and to develop diagnostic

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[1] Counsel for all parties have consented to the filing of this brief, and their consents have been lodged with the Clerk of this Court. No counsel for any party had any role in authoring this brief, and no person other than the named *amici* and their counsel has made any monetary contribution to the preparation and submission of this brief. *See* Rule 37.

methods for determining the patient population for which particular drugs are safe and effective.

Amicus Mohr, Davidow Ventures ("MDV") is a leading Silicon Valley-based venture capital firm specializing in predictive diagnostics and personalized medicine, as well as other areas that are dependent on fundamental innovation and invention. MDV works closely with life sciences entrepreneurs from academic institutions, like Stanford, Harvard, and MIT, who are passionate about inventing and commercializing novel technologies and business models that will transform the practice of medicine for the benefit of the ultimate consumers – physicians and patients. With its strong multidisciplinary scientific expertise, MDV brings 20 years of experience helping entrepreneurs build start-ups, and close involvement with industry and academic leaders in multiple health-care disciplines.

Like Perlegen, MDV has a strong interest in ensuring that Claim 13 is held to recite patentable subject matter. MDV believes that the health-care industry is on the cusp of a transformation in which more informative, personalized diagnostics will serve as a gateway to better, more efficient treatment and significantly reduce the waste and (all too frequently) loss of life associated with treatment of patients based on too little information. MDV has provided funding for a number of these next-generation diagnostics start-ups, in part in the knowledge that diagnostic methods similar to those set forth in Claim 13 have been consistently granted patent protection over an extended period of time. Any other holding with respect to Claim 13 could limit the economic viability of companies seeking to research and develop diagnostic methods like that identified in Claim 13, and thus could adversely affect the life

sciences companies for which MDV has provided investment backing. Moreover, if such methods are held unpatentable, MDV – indeed, venture capitalists in general – would have significantly diminished incentives to invest in the very companies that are on the forefront of research and development in personalized medicine and diagnostics.

SUMMARY OF ARGUMENT

Claim 13 recites patentable subject matter under 35 U.S.C. § 101. To satisfy the patentability test of § 101, a process claim must, when considered as a whole, identify subject matter that is useful and made by man, that is not simply a natural law, and that transforms a physical object into a different state or thing. That one step in a process may be unpatentable as a law of nature does not prevent the process itself from being patentable under § 101. Claim 13, which recites an assay-plus-correlation method for diagnosing cobalamin and folate deficiencies, easily satisfies these requirements.

Claim 13 as a whole performs a useful function – employing body fluid to diagnose these two deficiencies – that neither the assay step nor the correlation step alone could perform. This diagnostic tool is made by man because, in nature, it is impossible to diagnose such deficiencies through unaided inspection of body fluid. Even assuming that the correlation step is a natural law, the result of the process, a medical diagnosis, is not. The method identified in Claim 13 also transforms body fluid through physical and chemical alteration so that it may be injected into scientific instruments for measurement.

Because Claim 13 is self-limited to assays of body fluid, not body tissue, it does not preempt every substantial application of the asserted natural law. If this Court holds the subject matter of Claim 13 to be unpatentable, the validity of a vast number of well-known diagnostic patents – including tests for prostate cancer and HIV – would be in question, because all such tests involve, literally or substantively, a similar assay-plus-correlation method.

Should this Court nonetheless hold the subject matter of Claim 13 to be unpatentable, its holding should be narrow. This Court's cases extensively discuss patentable subject matter and already set appropriate limits on the scope of patentability. Any ruling in this case should not fundamentally alter those limits, particularly where, as here, the record is not fully developed, and any concern of the Court could be addressed by a more limited reading of "correlation" or by a minor modification of Claim 13.

A holding that Claim 13 does not recite patentable subject matter could upset the careful balance struck by Congress in the nation's patent laws. Granting patent protection for diagnostic-method claims creates strong incentives for research and development, while providing the public, and competing researchers and companies, with full mandatory disclosure concerning the patent's underlying details. Such disclosure can help, even spur, competitors to develop new improvements and methods. Without that incentive, researchers, companies, and investors will be unlikely to put their time and money into research and development of new diagnostic methods.

ARGUMENT

I. CLAIM 13'S COMBINATION OF THE ASSAY STEP WITH THE CORRELATION STEP IS PATENTABLE SUBJECT MATTER, EVEN ASSUMING THAT THE CORRELATION STEP ALONE IS NOT PATENTABLE

A. Claim 13 Recites Patentable Subject Matter

"[T]hat one or more of the steps in [a] process may not, in isolation, be novel or independently eligible for patent protection is irrelevant to the question of whether the claim[] as a whole recite[s] subject matter *eligible* for patent protection under § 101."[2] *Diamond v. Diehr*, 450 U.S. 175, 193 n.15 (1981) (emphasis in original). While a law of nature is not patentable, "a process is not unpatentable simply because it contains a law of nature." *Parker v. Flook*, 437 U.S. 584, 590 (1978). "It is now commonplace that an *application* of a law of nature . . . to a known . . . process may well be deserving of patent protection." *Diehr*, 450 U.S. at 187 (emphasis in original). The key is whether a useful invention has resulted: "He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such discovery, it must come from the application of the law of nature to a new and useful end." *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).[3] A combination of old or otherwise unpatentable

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[2] Claim 13, in identifying a "method," *see* SA 30, is a process claim. *See* 35 U.S.C. § 100(b) (defining "process" as, *inter alia*, "method").

[3] Although *Funk Bros. Seed Co.* concerned a product claim, its holding applies to a process claim. *See Diehr*, 450 U.S. at 188 n.11 (citing *Gottschalk v. Benson*, 409 U.S. 63, 68 (1972)). As a general matter, cases that respectively concern product and process claims may be cited interchangeably for the purpose of determining whether the

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elements can itself be patentable when "the whole in some way exceeds the sum of its parts." *Great Atl. & Pac. Tea Co. v. Supermarket Equip. Corp.*, 340 U.S. 147, 150-52 (1950).

Claim 13's combination of the assay and correlation steps is indisputably a useful invention, because it performs a function that neither step alone can perform. Neither of Claim 13's two steps can use body fluid to diagnose cobalamin or folate deficiency. Prior to the invention of the method recited in Claim 13, the assay step could result only in a determination of the level of a chemical substance, homocysteine, in the assayed body fluid. But that assay result was diagnostically useless with respect to either vitamin deficiency. (Insofar as an elevated level of homocysteine was theretofore associated with illness, it was associated primarily with heart disease.[4] Pet. Br. at 3.) Similarly, knowing the correlation between an elevated level of total homocysteine and a cobalamin or folate deficiency cannot permit a diagnosis of either deficiency because the correlation is unconcerned with, and offers no instruction regarding, testing of body fluid. SA 30. Rather, the correlation is abstract knowledge, unrelated to either alteration and examination of body fluid or to diagnosis of individual patients.

In combination, however, the assay and correlation steps result in a useful diagnostic method. Here, it cannot be reasonably doubted that the "whole in some way exceeds

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unpatentability of one step or element of a claim renders the entire claim unpatentable. *Benson*, 409 U.S. at 67-68.

[4] Elevated levels of total homocysteine are also associated with renal disease, vitamin B6 deficiency, hypothyroidism, and lupus. *See, e.g.*, JA 250-51, 336-38, 355-56.

the sum of its parts." *Great Atl. & Pac. Tea Co.*, 340 U.S. at 152, *quoted in Diehr*, 450 U.S. at 193 n.15. As in *Diehr*, the application of what is assertedly a natural law (the correlation of elevated total homocysteine to cobalamin or folate deficiency) to a known process (the assay) has yielded a method for diagnosing such deficiencies that can save lives. Under *Diehr*, the subject matter of Claim 13 is therefore patentable.

Patentable subject matter includes "'anything under the sun that is made by man.'" *Diehr*, 450 U.S. at 182 (quoting legislative history of Patent Act of 1952); *see also Cuno Eng'g Corp. v. Automatic Devices Corp.*, 314 U.S. 84, 90 (1941) (subject matter must be not only "useful," but also an "invention"). Petitioner's single-minded focus on natural law – that is, on the inclusion in the correlation step of an asserted law of nature – obscures not only the assay step but also the inventiveness and utility of the steps' combination. *See* Pet. Br. Point I.A. Because of the risk inherent in such myopic attention to only one step in a process, *Diehr* warns that a court, in determining whether the subject matter of a process claim is patentable, must consider the claim "as a whole." *Diehr*, 450 U.S. at 188. Considered "as a whole," Claim 13 clearly satisfies the requirement that its subject matter be "made by man." The first step in the process – the assay – is undisputedly "made by man."[5] More important, the *result* of the process as a whole cannot exist in nature, because of the impossibility of diagnosing cobalamin or folate deficiency through unaided inspection of body fluid. Thus, the result – a medical diagnostic – is "made by man," and

[5] The validity of Respondents' patent claims concerning particular homocysteine assays is undisputed. Pet. Br. at 31-32.

hence patentable. Moreover, medical diagnosis based on any assay of a sample of body fluid from a patient – the overall accomplishment of Claim 13 – is clearly *not* a law of nature or natural phenomenon.

Insofar as a process, to be patentable, must "transform[]" an article into a "different state or thing," *Diehr*, 450 U.S. at 183, 184, Claim 13 clearly passes this test. The process described in Claim 13 requires assaying a body fluid for total homocysteine. An assay of a body fluid for total homocysteine necessitates substantial chemical and physical alteration of that fluid. For example, as demonstrated by the Detailed Description in the patent at issue, *see* SA 13-20 (col. 7, line 23, to col. 9, line 29; Examples II & III), a body fluid, such as a blood sample, must be obtained and mixed with an internal reference, such as an isotopically labeled molecule that reacts in a manner similar to homocysteine. This mixture is reacted with one or more reagents that break chemical bonds in the sample to free bound homocysteine groups. Protein is then removed through one or more steps, such as heat denaturation, ion exchange chromatography, or protein precipitation. Salts are subsequently removed from the sample with cation and anion exchange columns. Thereafter, the amino acids are concentrated and derivatized by reaction with additional chemicals that attach multiple silyl-containing groups to them. The resultant mixture is evaporated almost to dryness and injected onto a gas chromatograph/mass spectrophotometer for measurement. SA 13-20. This measurement is then used to calculate the total homocysteine level for the body fluid sample. In view of these many alterations of the blood sample, Claim 13 taken "as a whole," *Diehr*, 450 U.S. at 188, clearly satisfies

the transformation requirement. Petitioner's argument to the contrary is simply mistaken. *See* Pet. Br. at 27.

The inclusion in Claim 13 of a step requiring such tangible manipulation of a physical object – *i.e.*, the assay – puts Claim 13 squarely in the realm of patentable subject matter. This was the precise holding of *Diehr*: "[W]hen a claim containing a mathematical formula implements or applies that formula in a structure or process which, when considered as a whole, *is performing a function which the patent laws were designed to protect (e.g., transforming or reducing an article to a different state or thing)*, then the claim satisfies the requirements of § 101." 450 U.S. at 192 (emphasis added). More may be required of the claim ultimately to make it patentable; for example, the combination of the tangible manipulation with the natural law must be novel and non-obvious, and must satisfy the description, enablement, and definiteness requirements. *See* 35 U.S.C. §§ 102, 103, 112. But to clear the threshold of § 101, nothing more is required. *See Flook*, 437 U.S. at 593 ("The obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious."). As the *Diehr* Court held: "In this case, it may later be determined that the respondents' process . . . fails to satisfy the statutory conditions of novelty under § 102 and nonobviousness under § 103. A rejection on either of these grounds does not affect the determination that respondents' claims recited subject matter which was eligible for patent protection under § 101." 450 U.S. at 191.

Finally, even assuming that the correlation step represents a natural law, Claim 13 does not seek to pre-empt all use of the natural law, and does not cover every "substantial practical application" of the natural law. *See*

Benson, 409 U.S. at 71-72 (claimed process that involves mathematical formula is unpatentable if process includes every "substantial practical application" of mathematical formula, such that "the patent would wholly pre-empt the mathematical formula and in practical effect be a patent on the algorithm itself."). Specifically, Petitioner asserts that step one of Claim 13 concerns *any* assay, and thus that there are no substantial practical applications of the natural law that are not included within Claim 13. Pet. Br. at 29. Petitioner is mistaken, however. The assay claimed in step one is only of body fluids, not of other tissues. *See* SA 30 (describing step one as "assaying a body *fluid* for an elevated level of total homocysteine" (emphasis added)). Respondents' patent specification references "assays capable of determining levels of homocysteine in *body tissues,* preferably *body fluids*. . . ." SA 12 (emphasis added).[6] This portion of the specification thus demonstrates that assays of non-fluid tissues exist, and, given Claim 13's reference to assaying a body "fluid," SA 30, that diagnoses based on non-fluid assays are "substantial practical application[s]" involving no infringement whatever.[7]

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[6] The specification makes numerous additional references to body "tissue" and body "tissues." *See* SA 1, 10, 11, 12. Claim 5 explicitly references assay of "body tissue," as opposed to "body fluid." SA 30. Because Respondents clearly knew the difference between assay of tissue and assay of fluid, and because Claim 13 recites only assay of fluid, one must conclude that Claim 13 unequivocally excludes non-fluid assays. Respondents' intentionally disparate use of language supports the contention that Claim 13 does not include this "substantial practical application" and thus does not preempt the asserted natural law contained in the correlation step.

[7] Although the *Flook* Court held that the respondent's claim there was not patentable under § 101, the Court's holding was not based on

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B. A Reversal Would Call Into Question Innumerable Patents for Diagnostic Methods

Virtually every patent claim concerning a diagnostic method is based, explicitly or implicitly, on a correlation between a test result and a disease or medical condition. Thus, the repercussions for biotechnology, particularly diagnostics, if the decision below were reversed would be staggering. Hundreds, if not thousands, of patents would at once be called into question. Furthermore, since the research and development necessary to "personalize" medicines would be obstructed, many drugs that would aid in human health could be left unused. In a similar context, the *Diehr* Court rejected the argument that a claimed process is not patentable when it combines a previously known process with a natural law – that is, when the only newly invented step is a natural law: "To accept th[is] analysis . . . would, if carried to its extreme, make all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious." 450 U.S. at 189 n.12.

Patents have routinely been granted for diagnostic methods that, like Claim 13, consist of a non-specific "assay" or other measurement, followed by a "correlation"

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preemption. Indeed, the Court agreed with the respondent's argument that there were uses of the respondent's formula outside the respondent's own industry and thus that the claim did not violate the preemption prohibition. 437 U.S. at 589-90. Because Claim 13 is self-limited to body-fluid assays and does not include non-fluid assays, Petitioner's assertions that Claim 13 has a "prohibited preemptive sweep," Pet. Br. at 28, and that "Claim 13 covers every total homocysteine test no matter how it is performed," Pet. Br. at 29, are simply incorrect.

or functionally similar activity. Some of the more well-known examples include:

- **Prostate Specific Antigen ("PSA") test for prostate cancer:** Claim 10 of U.S. Patent No. 5,840,501, assigned on its face to Bayer Corp., identifies a method consisting of any "immunoassays" followed by a "correlat[ion]": "A method for monitoring the course of disease in a male patient diagnosed with prostate cancer, comprising the performance of a series of *immunoassays* over time to determine changes in the level of complexed prostate specific antigen (cPSA) in blood samples obtained from such patient, whereby changes in the cPSA blood level *correlate* with changes in disease status." (Emphasis added.) PSA is widely used to determine if a man has prostate cancer.

- **Test for HIV/AIDS:** Claim 1 of U.S. Patent No. RE38352, assigned on its face to Stanford University, identifies a method consisting of any test for a specific nucleic acid mutation, followed by a "correlat[ion]": "A method of evaluating the effectiveness of antiretroviral therapy of an HIV-infected patient comprising: collecting a plasma sample from an HIV-infected patient; and *determining* whether the plasma sample comprises nucleic acid encoding HIV reverse transcriptase having a mutation at codon 215, in which the presence of the mutation *correlates* positively with an accelerated immunologic decline of said patient compared to patients who do not have the mutation." (Emphasis added.) Mutations in the HIV virus within an infected individual are widely used (including by LabCorp) to help people find and take drugs that will make them better, and to avoid drugs that will make them sicker.

- **HER-2/neu test for breast and ovarian cancer:** Claim 1 of U.S. Patent No. 4,968,603, assigned on its face to the University of California, identifies a method consisting of any test for the amplification level of the HER-2/neu gene, followed by "classifying" an increased amplification relative to a "reference level": "A method for screening patients to determine disease status, said method comprising: *measuring* the level of amplification or expression of the HER-2/neu gene in a sample from a patient suffering from breast or ovarian adenocarcinoma; and *classifying* those patients having an increased level of amplification or expression of the HER-2/neu gene relative to a reference level characteristic of normal cells as being more likely to suffer disease relapse or having a decreased chance of survival." (Emphasis added.) HER-2/neu-related tests are widely used to determine which drug should be taken by a woman with breast cancer.

- **Test for neoplastic (i.e., cancerous) tissue:** Claim 7 of U.S. Patent No. 5,955,263, assigned on its face to Johns Hopkins University and Genzyme Corp., identifies a method consisting of comparing normal and abnormal proteins, and detecting a mutation-based alteration in the amino acid sequence wherein the alteration "indicates" neoplasia: "A method to aid in determining neoplasia of a tissue of a human, comprising: *comparing* (a) p53 proteins in a human tissue suspected of being neoplastic to (b) wild-type p53 proteins in a normal tissue of said human; detecting an alteration in the amino acid sequence between the p53 proteins, wherein the alteration is due to a mutation in a p53 gene in the human tissue suspected of being neoplastic, wherein the mutation is selected from the group consisting of:

> a point, deletion, missense, and frameshift mutation, *wherein an alteration in the amino acid sequence indicates neoplasia*." (Emphasis added.) Science Magazine named p53 the "molecule of the year." Mutations in p53 help doctors determine whether a tissue is cancerous.

That these examples are so familiar attests to the importance of incentivizing inventors through patent protection. This is the basis of the patent system – to provide incentive for new discoveries and their disclosure. Indeed, the critically important inventions listed above would not exist but for the patentability of assay-plus-correlation methods like that identified in Claim 13. And these constitute not only a small sampling of the vast array of diagnostic-method patents jeopardized by Petitioner's argument, but also a modest reflection of all the future inventions that might never come into being if the Court holds the subject matter of Claim 13 to be unpatentable.

II. ANY RULING IN THIS CASE SHOULD BE NARROW AND SHOULD NOT UPSET SETTLED LAW ON PATENTABLE SUBJECT MATTER

As detailed above, *amici* Perlegen and MDV believe that Claim 13 recites patentable subject matter. If the Court holds otherwise, however, its ruling should be narrow. In its prior discussion of the scope of patentable subject matter, the Court, acknowledging the author of the nation's first patent statute, has emphasized that "[t]he subject-matter provisions of the patent law have been cast in broad terms to fulfill the constitutional and statutory goal of promoting 'the Progress of Science and the useful Arts' with all that means for the social and economic

benefits envisioned by Jefferson." *Diamond v. Chakrabarty*, 447 U.S. 303, 315 (1980).

The existing limits on patentability, which include exceptions for "laws of nature, natural phenomena, and abstract ideas," *Diehr*, 450 U.S. at 185, already serve to promote the goal of invention and to avoid unnecessary judicial entanglement.[8] Any ruling in this case should not upset this settled law. In particular, any ruling should not upset settled law that diagnostic-method claims – including those involving an assay and correlation, which are common and of vital importance – are valid and patentable.

The scope of patentability should not be altered through this case for several reasons. First, as *amicus* United States explains, the record in this case is not sufficiently developed to permit comprehensive consideration of § 101's patentability requirements. U.S. Br. Point B. In fact, Petitioner did not argue below that the relevant patent was invalid under § 101, and Respondents had neither reason nor opportunity to introduce evidence to attempt to defeat a challenge under § 101. *Id.* Points B, C.2.b. Likewise, questions regarding Claim 13's patentability (if there were any) might be easily addressed simply by narrowing the court of appeals' interpretation of "correlation" in the second step of the claim. *Id.* Point C.3.

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[8] Of course, numerous additional statutory criteria further guard against the improper grant of a patent for matters undeserving of such protection: the novelty requirement of 35 U.S.C. § 102, the non-obviousness requirement of 35 U.S.C. § 103, and the enablement, written description, and definiteness requirements of 35 U.S.C. § 112.

Second, even if Claim 13 did not recite patentable subject matter as currently drafted, a minor modification could render it so. For example, one could add the simple step – beyond the abstract mental correlation between homocysteine levels in assayed body fluid and a deficiency of cobalamin or folate – of performing the correlation by computer. In other words, a third step would involve inputting a number (homocysteine levels), performing a correlation via an algorithm, and outputting another number (probability of a cobalamin and/or folate deficiency). With such a step added, Claim 13 would be analogous to other claims found to recite patentable subject matter. *See State St. Bank & Trust Co. v. Signature Fin. Group, Inc.*, 149 F.3d 1368, 1373 (Fed. Cir. 1998) ("[T]he transformation of data . . . by a machine through a series of mathematical calculations into a final [number], constitutes a practical application of a mathematical algorithm, formula, or calculation, because it produces a 'useful, concrete and tangible result.'" (quoting *In re Alappat*, 33 F.3d 1526, 1544 (Fed. Cir. 1994)).

III. ANY RULING IN THIS CASE SHOULD NOT UPSET THE CAREFUL BALANCE STRUCK UNDER OUR PATENT SYSTEM

The Constitution gives Congress "broad power to legislate to 'promote the Progress of Science and useful Arts. . . .'" *Chakrabarty*, 447 U.S. at 307 (quoting U.S. Const. art. I, § 8, cl. 8). The nation's patent laws "promote this progress by offering inventors exclusive rights for a limited period as an incentive for their inventiveness and research efforts." *Id.* (citations omitted). "The authority of Congress is exercised in the hope that '[t]he productive effort thereby fostered will have a positive effect on society

through the introduction of new products and processes of manufacture into the economy, and the emanations by way of increased employment and better lives for our citizens.'" *Id.* (citation omitted). The Patent Act of 1793, authored by Thomas Jefferson and, in relevant part, continuing substantially unchanged to the present, "embodied Jefferson's philosophy that 'ingenuity should receive a liberal encouragement.'" *Id.* at 308 (quoting 5 Writings of Thomas Jefferson 75-76 (Washington ed. 1871)).

Our patent system is therefore based on a careful balancing of various interests: To provide incentives for individuals and companies to conduct research and develop inventions, the Patent Act grants a patentee a limited exclusivity (in this case, for 17 years from the patent's issuance) to practice its invention. At the same time, as a *quid pro quo* for this limited exclusivity, a patentee must disclose detailed information about the manner and process of making and using the invention. 35 U.S.C. § 112 ("The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."). This disclosure requirement, in turn, ensures that the public receives the benefit of the patentee's research and development and thus provides a basis and incentive for other inventors to develop additional inventions around the patented one. *See generally Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 63 (1998) ("[T]he patent system represents a carefully crafted bargain that encourages both the creation and the public disclosure of

new and useful advances in technology, in return for an exclusive monopoly for a limited period of time").[9]

Research for diagnostics and other aspects of human health is funded either in an academic setting or by industry. The health-care industry relies on the very economic incentives provided by our patent system, including in large part by the patentability of claims such as Claim 13. If such claims were subject to invalidation as unpatentable, health-care companies would lose incentive to conduct research into basic diagnostics, to develop

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[9] In *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470 (1974), Chief Justice Burger described the balance as follows:

> The stated objective of the Constitution in granting the power to Congress to legislate in the area of intellectual property is to "promote the Progress of Science and useful Arts." The patent laws promote this progress by offering a right of exclusion for a limited period as an incentive to inventors to risk the often enormous costs in terms of time, research, and development. . . . In return for the right of exclusion – this "reward for inventions" – the patent laws impose upon the inventor a requirement of disclosure. To insure adequate and full disclosure so that upon the expiration of the 17-year period "the knowledge of the invention enures to the people, who are thus enabled without restriction to practice it and profit by its use," the patent laws require that the patent application shall include a full and clear description of the invention and "of the manner and process of making and using it" so that any person skilled in the art may make and use the invention. 35 U.S.C. § 112. When a patent is granted and the information contained in it is circulated to the general public and those especially skilled in the trade, such additions to the general store of knowledge are of such importance to the public weal that the Federal Government is willing to pay the high price of 17 years of exclusive use for its disclosure, which disclosure, it is assumed, will stimulate ideas and the eventual development of further significant advances in the art.

Id. at 480-81 (internal citations and footnote omitted).

personalized medicine tools and diagnostic systems, to validate them, and to have them approved by the FDA – all steps that are tremendously costly and necessary for the public to derive any benefit from new diagnostics. Likewise, venture capital and other financial firms would no longer have incentives to fund or invest in health-care companies that pursue the research, development, and regulatory approval of drugs and diagnostic systems. If there is no expectation of a limited right to exclusivity, industry will respond: These areas will be neglected in favor of other areas for which patent protection is still available.[10]

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[10] Harm from declaring claims like Claim 13 unpatentable is not limited to the loss of incentives for research and development. Rather, the diagnostics segment of the biotechnology industry – which industry generated $46 billion in revenues and 187,500 jobs in 2004, and which had a market capitalization of $488 billion in November 2005 – could be seriously jeopardized. *See* G. Steven Burrill, *Burrill's Biotech Outlook for 2006* . . . and a Look Back at 2005, PR Newswire, Dec. 22, 2005, *available at* http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=109&STORY=/www/story/12-22-2005/0004238848&EDATE=; *Biotechnology Industry Facts*, Biotechnology Industry Organization (2006), *available at* http://www.bio.org/speeches/pubs/er/statistics.asp. As described *supra* in Point I.B, if Claim 13 were found unpatentable, numerous other two-step diagnostic patents could be rendered void. At a minimum, companies holding those patents – and their investors and financial backers – would face uncertainty as to the value of their patents and the corresponding value of their businesses. It is unquestionable that a biotechnology company's value drops precipitously upon expiration of its patents, demonstrating the economic value afforded by patent protection. For example, Merck recently announced that it expected sales of its top-revenue product, the cholesterol drug Zocor, to drop from $4.35 billion in 2005 to $2.45 billion in 2006, when its patent expires in June 2006. *See Merck Plans More Cost-Cutting*, N.Y. TIMES, Dec. 16, 2005 at C5. A ruling finding claims like Claim 13 unpatentable would hasten such reduction of value for numerous companies, with devastating effects for the biotechnology industry.

Our patent system has already reached the proper balance of rewards and limits, particularly with regard to two-step diagnostic claims like Claim 13. The "reward" of patent protection is granted for only a limited time. The '658 patent, for example, expires in 2007. After that time, the patented method is freely available to the public. In addition, the reward is conditioned on disclosure of what has been invented – spurring competitors to search for other, better ways of achieving the same result. Indeed, such incentivized innovation is easily demonstrated in this case. Others in the field may use the detailed information disclosed by the '658 patent to help them design other, better methods to make the diagnosis of a cobalamin or folate deficiency – perhaps by using non-homocysteine markers, or by assaying homocysteine in a sample that is not a body fluid, or by some other entirely different method. At the same time, without the incentive of patent protection, an inventor would keep its knowledge secret, providing no benefit to the public.[11]

The ruling urged by Petitioner and various *amici* would upset the careful balance under our patent system. Indeed, their assertions ignore crucial aspects of the balance that has been struck – including the limited nature of patent protection and the full disclosure condition.

Contrary to Petitioner's suggestion, *see, e.g.*, Pet. Br. Point III, patent claims such as Claim 13 do not threaten doctors and never have. Claims in which a natural phenomenon is one, but not every, element of the claim are

[11] In addition, there would be no limit on how long the inventor may or would keep the knowledge from the public.

common. No doctor, however, has been sued for infringement of such a claim. The defendant in the instant case is Laboratory Corporation of America Holdings, a large industrial concern that profits from its vigorous marketing, promotion, and sale of an assay method that infringes the '658 patent.

Petitioner also wrongly hypothesizes that claims such as Claim 13 will lead to a decrease in testing and treatment. Pet. Br. Point III. To the contrary, testing and treatment are improving at an accelerating pace, due in large part to the incentives provided by patents. Following the successful sequencing of the human genome, new products are entering the market at a rapid pace. The future will see a large increase in diagnostics for cancer, genetic diseases, Alzheimer's disease, rheumatoid arthritis, cardiovascular disease, diabetes, osteoporosis, and schizophrenia. Numerous markers for cancer are being identified and commercialized. New markers for prostate cancer, such as PCA3, have been identified, and a new test is being developed for the prediction of breast cancer recurrence.[12]

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[12] *Amicus* American Clinical Laboratory Association ("ACLA") argues that a decision holding Claim 13 patentable would have inhibited testing such as that based on the correlation of increased risk of coronary heart disease with elevated blood levels of low-density lipoprotein ("LDL"), or testing based on the correlation of the presence of prostate cancer with an elevated level in body fluids of PSA. ACLA Br. Point II. Again, as an initial matter, doctors are not now being – and have never been – sued for infringement of diagnostic patents. In any event, if the patents envisioned by *amicus* had existed, they would have long since passed into the public domain due to the time limitation on patent protection. In addition, if the hypothetical patents had existed, the doomsday scenarios posited would not have been the necessary outcomes. Instead, with respect to LDL, the outcome could well have

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Similarly unavailing is Petitioner's contention that, "[i]f claim 13 is upheld, anyone who claims to be the first to discover a correlation can patent it – and thereby demand a royalty from anyone who even thinks about it. . . ." Pet. Br. at 46. As an initial matter, Claim 13 does not encompass a mere correlation; it is a two-step claim, one step of which includes a correlating step. In addition, "anyone who claims to be the first to discover a correlation" cannot obtain a patent solely for the correlation. Even a process with further steps, such as Claim 13, is subject to scrutiny for additional criteria: novelty, non-obviousness, proper inventorship, written description, enablement, and disclosure of best mode, all of which must be satisfied before a patent issues. In any event, as this case demonstrates, no royalty is being sought from a "thinker," whether a physician or an academic. Rather, the royalty is being sought from a corporate entity that profits from its marketing, promoting, and sale of tests that infringe the relevant patent. Meanwhile, it is the existence of the patent – encouraging invention and the concomitant required disclosure to obtain a patent – that promotes the very "thinking" sought by Petitioner. Without patent

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been an acceleration in the pace to find new predictors and markers for heart disease. If there had been a patent on the LDL method, it is entirely possible that more sophisticated, improved methods (*e.g.*, methods taking into account both LDL and high-density lipoprotein) would have been available to the public far earlier. Moreover, with respect to PSA, there have been many patented methods to make improvements in the assay – undoubtedly prompted by the hope of finding better, more reliable diagnostic methods to which an inventor would have a limited proprietary right. These existing patents, in turn, are encouraging the development of the next generation of PSA assays, as well as the development of completely new methods of detecting prostate cancer.

protection for claims such as Claim 13, those in the industry who discovered such methods would keep them secret and no one else – whether doctor, academic, or competitor – would have the benefit of such information. As a result, others would likely not be in a position to improve the assay or to find a different way to diagnose cobalamin or folate deficiency so that a new patent might issue for the improvement or new diagnostic.[13]

Petitioner and several *amici* also argue that claims such as Claim 13 chill research. Again, just the opposite is the case: Claim 13 provides incentive to develop better homocysteine assay methods. Such methods – additional, improved versions of patented methods – are routinely patented. A different and improved homocysteine assay is precisely what Claim 13 does not cover and could be patented by anyone who invented it. In addition, Claim 13 provides incentive to research and develop further diagnostics for cobalamin or folate deficiency that do not depend on homocysteine. Meanwhile, any remaining concern regarding infringement liability for researchers can be addressed through already-existing or new exceptions to patent liability, including for experimental use, *see Deuterium Corp. v. United States*, 19 Cl. Ct. 624, 631 (1990); clinical research, *see Merck KGaA v. Integra Lifesciences I, Ltd.*, 125 S. Ct. 2372 (2005) (discussing 35 U.S.C. § 271(e)); or medical use, *see* 35 U.S.C. § 287(c). Particularly in the case of clinical research, the exception is extremely broad. The exclusivity of Claim 13 – which ends in less than a year – can also be mitigated through

[13] In addition, Petitioner's concerns can be addressed, in any particular case, through the proof required to show direct infringement and the scope of any injunction entered.

cross-licensing, a daily phenomenon in the biotechnology industry. For example, anyone who invents a better assay can patent it and create leverage to cross-license the '658 patent, thus gaining access to patent rights.[14]

Finally, the discussion above demonstrates the weighty policy issues underlying our carefully structured and long-standing patent system. As shown in Point I, *supra*, Claim 13 fits easily within § 101's existing requirements for patentability. While Petitioners ask the Court to change this framework and to impose a further limitation on patentability, any such revision should be left to the Legislative branch. This Court so stated in *Chakrabarty*:

> The choice we are urged to make is a matter of high policy for resolution within the legislative process after the kind of investigation, examination, and study that legislative bodies can provide and courts cannot. That process involves the balancing of competing values and interests, which in our democratic system is the business of elected representatives. Whatever their validity, the contentions now pressed on us should be addressed to

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[14] The policy arguments proffered by *amici* Affymetrix and Professor Barton are generally directed at patentability of composition claims (and specifically claims covering isolated genes). *See* Affymetrix/Barton Br. Point II.B. There are strict, court-sanctioned Patent and Trademark Office Utility Guidelines for patenting a gene: The gene must be isolated out of its natural setting, and there must also be considerable evidence that the patentee understood the nature of the gene product coded for by the gene and its significance in physiological and biochemical function. *See In re Fisher*, 421 F.3d 1365, 1372-76 (Fed. Cir. 2005). The issue in the present case, however, is the patentability of a diagnostic-method claim, Claim 13. Case law regarding the patentability of method claims that include a natural phenomenon (*e.g.*, *Diehr*) focuses on a step-by-step method.

> the political branches of the Government, the Congress and the Executive, not to the courts.

447 U.S. at 317; *cf. Diehr*, 450 U.S. at 182 ("courts 'should not read into the patent laws limitations and conditions which the legislature has not expressed'").[15] Any ruling in this case should not upset settled law and expectations concerning the scope of patentability, and any limitation on the scope of patentable subject matter in the particular context of diagnostic claims should be left to Congress.

CONCLUSION

The judgment of the court of appeals should be affirmed.

Respectfully submitted,

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[15] Congress can and does amend the patent law when it finds that a change is in the public interest. For example, in 1996, Congress exempted certain medical activity from giving rise to infringement liability. 35 U.S.C. § 287(c) (added by Pub. L. No. 104-208, § 616, 110 Stat. 3009, 3009-67 (Sept. 30, 1996)).